

Thiol의 친핵성 첨가물의 합성 (제VIII보)
 β -Acetyl- β -benzoylstyrene 유도체에 대한 thioglycolic acid,
benzenethiol 및 benzylmercaptan 첨가 생성물의 합성

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Synthesis of Nucleophilic Adducts of thiols (VIII).
Addition of Thioglycolic acid, Benzenethiol and
Benzylmercaptan to β -Acetyl- β -benzoylstyrene Derivatives

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요 약. β -Acetyl- β -benzoylstyrene 유도체에 대한 thioglycolic acid, benzenethiol 및 benzylmercaptan의 첨가반응에 관하여 연구하였다. β -acetyl- β -benzoylstyrene 유도체는 쉽게 thioglycolic acid, benzenethiol, benzylmercaptan과 반응하여 다섯가지 (2-acetyl-2-benzoyl-1-phenylethyl)thioglycolic acid 유도체 (IIa-IIe), 다섯가지의 (2-acetyl-2-benzoyl-1-phenylethyl)benzenethiol 유도체 (IIIa-IIIe) 및 다섯가지의 (2-acetyl-2-benzoylphenylethyl)benzylmercaptan 유도체 (IVa-IVe)를 합성한다.

ABSTRACT. The addition reactions of thioglycolic acid, benzenethiol and benzylmercaptan to β -acetyl- β -benzoylstyrene were investigated. β -Acetyl- β -benzoylstyrene derivatives easily underwent addition reactions with thioglycolic acid, benzenethiol, and benzylmercaptan to form five (2-acetyl-2-benzoyl-1-phenylethyl)thioglycolic acid derivatives (IIa-IIe), five (2-acetyl-2-benzoyl-1-phenylethyl)benzenethiol (IIIa-IIIe) derivatives and five (2-acetyl-2-benzoyl-1-phenylethyl)benzylmercaptan derivatives (IVa-IVe), respectively.

INTRODUCTION

Nucleophilic addition to the double bond of activated olefins is an important elementary process in organic chemistry¹⁻² and recently the kinetic studies are carried out systematically³. However, not much systematic work for the isolation of nucleophilic adducts has been done.

The addition of thiols to α , β -unsaturated

compounds is interesting because much information has appeared in the literatures⁴⁻⁷ concerning the antiviral and antitumor activities of their adducts.

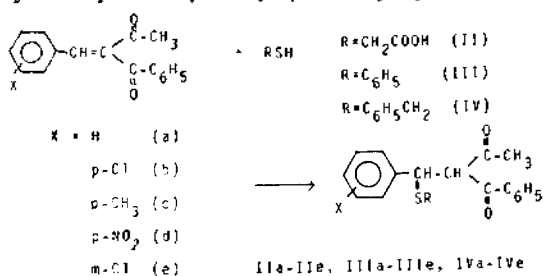
In the previous paper, nucleophilic adducts of thiols to β -nitrostyrene⁸, ω , ω -diacetylstyrene⁹ and α -cyano- β -phenylacrylic acid derivatives¹⁰ have been reported.

Table 1. Physical, analytical and spectral data of thioglycolic acid adducts to β -acetyl- β -benzoylstyrene derivatives

derivatives	mp(°C)	ir(cm ⁻¹)	nmr (ppm)	Elemental analysis		Neutralization Eq.		yield (%)
				Calcd. (%)	Found (%)	Calc.	Found	
H (IIa)	218~ 220	2900~3400 (broad) 1660 1720	2.36(s, $\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$)	for C ₁₉ H ₁₈ O ₄ S		342.42	346.37	76
			3.02(s, CH ₂ COOH)	C, 66.64	C, 67.37			
			5.04(m, CH-CH)	H, 5.29	H, 5.68			
			7.14~8.04(m, Ph)					
<i>p</i> -Cl (IIb)	113~ 115	2900~3400 (broad) 1650 1710	2.42(s, $\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$)	for C ₁₉ H ₁₇ O ₄ SCl		376.87	381.46	93
			3.04(s, CH ₂ COOH)	C, 60.55	C, 61.67			
			5.06(m, CH-CH)	H, 4.55	H, 4.86			
			7.00~7.98(m, Ph)					
<i>p</i> -CH ₃ (IIc)	221~ 223	2900~3500 (broad) 1660 1720	2.18(s, CH ₃ -Ph)	for C ₂₀ H ₂₀ O ₄ S		356.45	358.27	70
			3.02(s, CH ₂ COOH)	C, 67.39	C, 59.76			
			5.08(s, CH-CH)	H, 5.66	H, 6.39			
			7.23~8.23(m, Ph)					
<i>p</i> -NO ₂ (IIId)	108~ 109	2900~3500 (broad) 1650 1720	2.32(s, $\overset{\text{O}}{\parallel}{\text{C}}-\text{CH}_3$)	for C ₁₉ H ₁₇ O ₆ SN		387.42	385.65	98
			3.02(s, CH ₂ COOH)	C, 58.90	C, 59.76			
			5.08(s, CH-CH)	H, 4.42	H, 4.74			
			7.23~8.23(m, Ph)					
<i>m</i> -Cl (IIe)	123~ 124	2900~3500 (broad) 1970 1730	2.40(s, COCH ₃)	for C ₁₉ H ₁₇ O ₄ SCl		376.87	378.36	60
			3.04(s, CH ₂ COOH)	C, 60.55	C, 62.26			
			5.06(s, CH-CH)	H, 4.55	H, 5.36			
			7.03~8.02(m, Ph)					

RESULTS AND DISCUSSION

The β -acetyl- β -benzoylstyrenes were prepared by the reaction of benzaldehyde derivatives and benzoylacetone. Then the nucleophilic adducts were prepared by the typical Michael type reaction of thioglycolic acid, benzenethiol and benzylmercaptan to β -acetyl- β -benzoylstyrene deri-



vatives. Since the compounds, (Ia-Ie) were no longer the conjugated system by forming the adducts, the products were easily confirmed by IR and NMR spectral data. Physical and chemical data of thioglycolic acid, benzenethiol and benzylmercaptan adducts were recorded in Table 1, 2 and 3 respectively. The absorption at 1600 cm⁻¹ (C=C stretching) disappeared and a broad band at 2500~3300 cm⁻¹ appeared, which is attributable for carboxylic OH in thioglycolic acid adducts. Two doublets at 4.30 and 4.80 ppm (CH-CH) were observed in the adduct. A singlet at 3.06 ppm (*S*-CH₂COOH) in thioglycolic acid adducts and a singlet at 3.38 ppm (SCH₂C₆H₅) in benzylmercaptan adducts were

Table 2. Physical, analytical and spectral data of benzenethiol adducts to β -acetyl- β -benzoylstyrene derivatives

derivatives	mp ($^{\circ}$ C)	ir (cm^{-1})	nmr (ppm)	Elemental analysis		yield (%)
				Calcd (%)	Found (%)	
H (IIIa)	138~139	1650 1700	2.26(s, COCH ₃) 5.02(m, CH-CH) 6.98~7.87(m, Ph)	for C ₂₃ H ₂₀ O ₂ S C, 76.63 H, 5.59	C, 78.50 H, 5.70	76
<i>p</i> -C I(IIIb)	139~140	1660 1700	2.25s(, COCH ₃) 4.98(m, CH-CH) 6.98~7.87(m, Ph)	for C ₂₃ H ₁₉ O ₂ SCl C, 69.95 H, 4.85	C, 71.60 H, 5.04	84
<i>p</i> -CH ₃ (IIIc)	69~70	1650	2.12(s, CH ₃ Ph) 2.27(s, COCH ₃) 5.04(s, CH-CH) 6.90~7.95(m, Ph)	for C ₂₄ H ₂₂ O ₂ S C, 76.97 H, 5.92	C, 78.32 H, 6.06	80
<i>p</i> -NO ₂ (III d)	140~141	1650 1700	2.21(s, COCH ₃) 5.02(s, CH-CH) 7.05~7.95(m, Ph)	for C ₂₃ H ₁₉ O ₄ SN C, 68.13 H, 4.75	C, 69.46 H, 4.91	88
<i>m</i> -Cl (IIIe)	111~112	1650 1690	2.20(s, COCH ₃) 4.95(s, CH-CH) 6.80~7.88(m, Ph)	for C ₂₃ H ₁₉ O ₂ SCl C, 69.95 H, 4.85	C, 70.64 H, 4.76	71

observed.

In addition to the spectral data, melting point, elemental analyses, neutralization equivalents and yields were listed in Table 1, 2 and 3.

EXPERIMENTAL

All melting points are uncorrected. Infrared spectra were obtained on a Beckman AccuLab4 spectrophotometer. Proton NMR spectra were obtained on a Bruker WP 80 CW (80MHz) using TMS as the internal standard and chemical shifts are expressed in ppm unit. Neutralization equivalents were determined by a potentiometric titration with 0.092 *N* sodium hydroxide solution.

S-(2-Acetyl-2-benzoyl-1-phenylethyl)thioglycolic acid (IIa)

A mixture of β -acetyl- β -benzoylstyrene (2.5g, 0.01mol), sodium ethoxide (0.34g, 0.005mol) and thioglycolic acid (1.84g, 0.02mol) in ethanol (20ml) was stirred at 16 $^{\circ}$ C. After stirring

for 10 hours at the same temperature, cold dilute hydrochloric acid was added to the solution. The mixture was allowed to stand overnight. The resulting precipitates were collected by filtration. Recrystallization from CCl₄ gave white crystal of *S*-(2-acetyl-2-benzoyl-1-phenylethyl)thioglycolic acid (2.6g, 76%): mp 218~224 $^{\circ}$ C.

Spectral data, elemental analyses, neutralization equivalents and yields of *S*-(2-acetyl-2-benzoyl-1-phenylethyl)thioglycolic acid derivatives (IIa-IIe) were listed in Table 1.

S-(2-Acetyl-2-benzoyl-1-phenylethyl)benzenethiol(IIIa)

A mixture of β -acetyl- β -benzoylstyrene (2.5g, 0.01mol), triethylamine (0.5g, 0.005mol) and benzenethiol (1.1g, 0.01mol) in methanol (20ml) was stirred at 10 $^{\circ}$ C.

After stirring for 6 hours at the same temperature, dilute hydrochloric acid was added to the solution. The mixture was allowed to stand overnight. The resulting precipitates were

Table 3. Physical and spectral data of benzylmercaptan adducts to β -acetyl- β -benzoylstyrene derivatives

derivative	mp (°C)	ir (cm ⁻¹)	nmr (ppm)	Elemental analysis		yield (%)
				Calcd (%)	Found (%)	
H(IVa)	137~138	1670 1720	2.06(s, COCH ₃)	for C ₂₄ H ₂₂ O ₂ S		98
			3.32(m, SCH ₂)	C, 76.97	C, 78.12	
			4.52(d, CH-CH)	H, 5.92	H, 6.04	
			5.04(d, CH-CH)			
			7.12~7.98(m, Ph)			
<i>p</i> -C I(IVb)	121~122	1670 1720	1.98(s, COCH ₃)	for C ₂₄ H ₂₁ O ₂ SCl		78
			3.22(m, SCH ₂)	C, 70.48	C, 71.56	
			4.25(d, CH-CH)	H, 5.18	H, 5.36	
			4.61(d, CH-CH)			
			6.92~7.65(m, Ph)			
<i>p</i> -CH ₃ (IVc)	119~120	1670 1710	1.98(s, COCH ₃)	for C ₂₆ H ₂₄ O ₂ S		77
			2.12(s, CH ₃ Ph)	C, 77.28	C, 78.46	
			3.23(m, SCH ₂)	H, 6.23	H, 56.46	
			4.25(d, CH-CH)			
			4.82(d, CH-CH)			
<i>p</i> -NO ₂ (IVd)	113~136	1670 1720	1.96(s, COCH ₃)	for C ₂₄ H ₂₁ O ₄ SN		78
			3.31(m, SCH ₂)	C, 68.71	C, 69.56	
			4.45(d, CH-CH)	H, 5.26	H, 5.05	
			4.85(d, CH-CH)			
			7.02~7.98(m, Ph)			
<i>m</i> -Cl (IVe)	104~105	1660 1710	1.90(s, COCH ₃)	for C ₂₄ H ₂₁ O ₂ SCl		73
			3.25(m, SCH ₂)	C, 70.48	C, 71.68	
			4.15(d, CH-CH)	H, 5.18	H, 5.36	
			4.75(d, CH-CH)			
			6.95~7.80(m, Ph)			

collected by filtration. Recrystallization from benzene gave white crystal of *S*-(2-acetyl-2-benzoyl-1-phenylethyl)benzenethiol (2.74g, 76%): mp 138~139°C. Spectral data, elemental analyses and yields of *S*-(2-acetyl-2-benzoyl-1-phenyl-ethyl)benzenethiol derivatives(IIIa-IIIe) were listed in Table 2.

S-(2-acetyl-2-benzoyl-1-phenylethyl)benzylmercaptan (IVa)

A mixture of β -acetyl- β -benzoylstyrene(2.5g, 0.01 mol), triethylamine (0.5g, 0.005 ml) and benzylmercaptan(1.248g, 0.01 mol) in methanol (20ml) was stirred at 10°C.

After stirring for 3 hours, dilute hydrochloric acid was added to the mixture. The resulting precipitates were collected by filtration. Recrystallization from benzene gave white crystal of *S*-(2-acetyl-2-benzoyl-1-phenylethyl)benzylmercaptan (3.67g, 98%): mp 137~138°C. Spectral data, elemental analyses and yields of *S*-(2-acetyl-2-benzoyl-1-phenyl-ethyl)benzylmercaptan derivatives (IVa-IVe) were listed in Table 3.

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